REMARKS

The last Office Action of April 29, 2010 has been carefully considered. Reconsideration of the instant application in view of the foregoing amendments and the following remarks is respectfully requested.

Claims 56-60, 66-71, 75, 78-82 and 84-87 are pending in the application. Claims 66, 67, 69, 71, 75 and 87 have been amended. New claims 88, 89 and 90 are presented. A total of 22 claims is now on file. No amendment to the specification has been made. The fee for two new dependent claims is submitted herewith.

It Is noted that the Examiner objected to claims 56-60, 66-67, 69-71.

It is further noted that claims 56-60, 66-67, 69-71, 75, 78-82, 84, 86 and 87 are rejected under 35 U.S.C. §112, first paragraph as failing to comply with the written description requirement.

Claim 75 and 87 were rejected by the Examiner based on new matter.

Claims 56-60, 66-67, 69-71, 75, 78-82, 84, 86 and 87 as failing to comply with the written description requirements.

Claims 56-60, 66-67, 69-71, 75, 78-82, 84, 86 and 87 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 56-60, 66-67, 69-71, 75, 78-82, 84 and 86-87 stand rejected under 35 U.S.C. §102(e) as being anticipated by or in the alternative as obvious under 35 U.S.C. §103(a) over U.S. Patent 6,028,189 to Blanchard ("Blanchard").

Claims 56-60, 66-67, 69-71, 75, 78-82, 84 and 86-87 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Blanchard in view of Zebala of record and US Patent 7,179,638 to Anderson ("Anderson").

PRIORITY

A claim of priority was part of the application at all times. On September 15, applicant filed Priority documents including English translations. According to the priority documents an earliest date of priority is December 14, 1998.

CLAIM OBJECTION

The Examiner's objection is confusing and not understood. The citation of MPEP § 608.01(n) relates to claims of multiple dependencies. There are no multiple dependent claims in the application. The Examiner states that the claims have to refer to the preceding claim. As far as the Examiner's objection is understood, new independent claims were introduced after some former independent claims were cancelled. Needless to say that the former dependent claims now must depend from the independent claim of a higher number. If this does not eliminate the objection, the Examiner is respectfully requested to explain the objection further.

NEW MATTER REJECTION

The Examiner again issued a new matter rejection on terms that have either synonymous meaning or were chosen to make the claims more understandable in view of the continued rejections on what seems to be the same objections and has

rejected claim 75 and 87 based on the terms the Examiner states were not in the initial disclosure.

Applicant disagrees with this assessment. On numerous occasions the Examiner rejection prompted a rewording of the claims by applicant which then were met with new matter rejection.

The terms offensive to the Examiner are all referred to in the initial disclosure.

1) see claim 15 of the initial disclosure. The "embedding of the monomers within a solvent" is clearly from the original claims. Applicant is not required to state everything *verbatim* from the specification in the claims. Other paragraphs in the application refer to "dissolving" "immobilizing", "incorporated" "contained" are used synonymously. Claim 15 of the initial disclosure uses the term "embedding into a matrix". If it is clear from the disclosure including the claims initially filed that the term is not new matter. The embedding process is clearly outlined in the specification in [0125]. Others are found in [0024], [0029], [0037], [0049], [0055], [0057], [0093], [0095], [0123]. Issue is taken with the Examiner's repeated objection to the same wording, especially that the Examiner questions how monomers can be embedded in a solid solvent. Applicant has provided repeatedly references to "matrix" including that the matrix is shown in Figure 25 and referred to in the description to Figure 25 in the specification.

2) this terms is also clear from the context and from claim 15 of the initial disclosure that non-linked substances are washed away; see also [0026], [030], [0093], [0102], [0134], [0135] and [0142] - [0156]. To avoid confusion, applicant has eliminated the term "transport units" to make the claim clearer.

3) that term is also disclosed in the original application claim 15. From the context of the entire description the term transport units is entirely clear.

4) Applicant is at a loss to understand the new matter rejection since the wording the Examiner considers is not mentioned. The Examiner should specify the terms the Examiner deems new matter in claim 87 and discuss them, so that applicant can respond.

Applicant notes that the instant application was handled by a number of Examiner's and has been pending for more than 9 years. It is not understood why at this stage why applicant has to explain *again* every term used in the claims.

REJECTION OF CLAIMS 56-60, 66-67, 69-71, 75, 78-84, 86 AND 87 UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Applicant addresses the Examiner's rejections in accordance with the numbered paragraphs in which they appear.

The Examiner is directed to [0123] and [0125] for the dissolving of he monomers into the solvent at the specified temperatures. Once the solvent is solid again, the monomers are deemed to be embedded.

The Examiner states that it is not apparent from the disclosure how the different monomers are embedded within the solvent. Applicant points to [023], [057] to [059] and [0123] to [0127]. The characteristics of the solvent are given in [023].

The printing method is stated in [093] and the operation of the laser printer in [096]

The description of the dissolution of the monomers in the solvent and the

preparation of toner particles is amply described in [095], [0123] and [0125] in which various methods are described how the toner particles are made.

The Examiner is directed to the fact that the invention does not rest in the solvent *per se* but in the fact that a phase shift can be accomplished by creating these transport units with various solvents that have the stated criteria in order to immobilize and then mobilize the monomers to diffuse them on the support for the combinatorial libraries.

The Examiner cites the *Eli Lilly* case which relates to c-DNA of mammalian insulin. Applicant submits that the Lilly case involved obscure and complex biological compounds, while here, solvents are known substances in the chemical fields, such that a solvent having certain characteristics are easily available.

In summary, applicant contends that the description contains everything to practice the invention.

In view of the foregoing, it is believed that all terms in the claims and all claim steps are referred to and explained in the specification. Withdrawal of the rejection of claims 56-60, 66-67, 69-71, 75, 78-84, 86 and 87 is thus respectfully requested.

REJECTION OF CLAIMS 56-60, 66-67, 69-71, 75, 78-84, 86 AND 87 UNDER 35 U.S.C. §112, SECOND PARAGRAPH

1. With respect to claim 75, "such as" has been eliminated.
2. As far as the rejection has been understood, applicant has formerly amended the claim to included the step, such that the Examiner's

rejection is duplicative.

3. The embedding into the matrix or the dissolving into the solvent has been amply discussed in the previous section and further below.

4. The term "defined" has been explained in several responses. The Examiner is directed to [0114] to [0137] for a comprehensive outline of the defined locations.

5. The Examiner is mistaken that the cited terms are used interchangeably. The solid solvent is just that, while the transport units are merely a conceptual use of a term to clarify what happens when the monomers are dissolved in the solvent or for that matter what happens when the monomers are "embedded in the matrix". "Transport units" are used to transport the embedded and immobilized monomers [0122] to [0125] to their address which is referred to in the specification at [026], [027], [038], [041] – [045], [052] – [056], [093], [95] – [099], [0116] and [0122] – [0125]. These expressions are totally within the realm of the invention and the proper expression thereto and were disclosed in the original application. The Examiner's objection to the way applicant drafted the claim after numerous rejections based on the term "matrix" is unfair.

6. The Examiner has objected to the term "repeatedly applying" as vague and indefinite. While applicant disagrees with this assessment, for efficiency's sake, applicant has amended claim 87 to reword the phrase, which is believed to be clear and definite. Support is found in [0026].

7. Applicant has changed the term "deep-frozen" to "frozen". While the specification recites "deep-frozen", the term frozen is incorporated

therein.

8. The Examiner is directed to the specification at [025], [057], [0123], [0131], [0133], and elsewhere for the specific derivatives that are set forth there. "Derivatives" in the context used refer to specific compounds and those skilled in the art would have no problem understanding it in this context.

9. Claim 67 has been amended.

10. Claim 69 has been amended.

11. Claim 71 has been amended. Support for this amendment is found in [0030].

12. Applicant states that "matrix" was part of claim 15 as originally filed. "Matrix" is also found in Figure 25 which has been in the original application and which the Examiner repeatedly claims as not being in the application. Applicant has contacted the Examiner to ascertain that Figure 25 is before the Examiner and the Examiner has confirmed that Figure 25 is in the application. The description to FIG. 25 is also in the specification. "Matrix" was also listed in the National Phase application on the numeral list. "Matrix" is for example defined among others as "a mass by which something is enclosed or embedded". See Webster Third New International Dictionary. Here, the matrix includes the solvent. Important is that the monomers are embedded therein in a solvent. The matrix can thus just include the solvent or it could also have other components, not important or critical here.

If the Examiner has issues with the term "matrix", they should be more

clearly stated because the specification and the Figures and the original claims contain the term, which is clearly understood by the person skilled in the art. Applicant has amended claim 75 to read on dissolving the monomers in a solvent, however, applicant has retained the term "embedded in a matrix" in claim 87.

13. The Examiner's determination that steps are missing in claim 87 is not readily understood. Clarification is respectfully requested.

14. The Examiner's assessment of "suitable" in this context appears misplaced. The suitability is determined by those skilled in the art of what it is that should be investigated by a combinatorial synthesis of molecule libraries. In this context it is up to the person who investigates the molecules who determines what is suitable for investigation. The use here is similar to a phrase used in the context of a pharmacological compound which is combined with a "suitable" carrier to be administered, to use an analogy. Therefore, the choice is up to the person carrying out the molecule library what monomers are desired to be used for the combinatorial synthesis of molecule libraries.

It is believed that based on the foregoing and the respective amendment that the rejection under 35 U.S.C. §112, second paragraph has been overcome.

Withdrawal of the rejection of claims 56-60, 66-67, 69-71, 75, 78-84, 86 and 87 under 35 U.S.C. §112, second paragraph is thus respectfully requested.

REJECTION OF CLAIMS 56-60, 66-67, 69-71, 75, 78-84, 86 AND 87 UNDER 35 U.S.C. §102(e) AS BEING ANTICIPATED BY OR IN THE ALTERNATIVE AS OBVIOUS UNDER 35 U.S.C. §103(a) OVER BLANCHARD

The Examiner's rejection of the claims is respectfully traversed. The Blanchard reference cannot anticipate the claimed invention, because Blanchard discloses and claims the use of an inkjet pump for its method.

A reference does not anticipate a claim unless each and every element of the claim is recited in the reference. This not he case here. In each of the independent claims 75, 80 and 87 a laser printer is recited in the method. Because Blanchard unequivocally uses the ink jet pump, claims 75, 80 and 87 are not anticipated by Blanchard. Since the dependent claims include each and every element of the independent claims, these claims are likewise not anticipated by the Blanchard reference.

Withdrawal of the claim as anticipated by Blanchard is thus respectfully requested.

The Examiner has in the alternative rejected the claims as being obvious over the Blanchard reference.

Blanchard uses a high surface tension solvent for the combinatorial synthesis of oligonucleotide array. The high surface tension solvent is exemplified in Fig. 1a. The reason for using high surface tension solvent is stated as "very small reagent droplets can be localized and separated from each other" "and act as miniature reaction vessels for oligonucleotide synthesis". Surface tension is the property of a liquid to resist an external force. Blanchard is thus in line with the

conventional combinatorial synthesis methods, except the ability to localizing and separating small reagent droplets.

The Blanchard method is entirely distinguishable from the above method. Blanchard does not teach that the (high-tension) solvent is in a solid state or a monomer could be embedded into the solvent in a solid state of aggregation. Blanchard does not teach that a high-tension solvent could be used as an undercooled liquid, nor does Blanchard teach to work below -49°C, where propylene carbonate is an undercooled liquid as claimed by the Examiner. Blanchard merely dissolves the monomers in propylene carbonate under standard conditions "by substituting a known coupling buffer or solvent with a high surface tension solvent", col. 5, lines 47-57.

Blanchard does not embed monomers in a solid state of aggregation, as suggested by the Examiner.

Blanchard does not teach the use of a laser printer for delivering monomers to the surface, as implied by the examiner, Blanchard instead uses "microfabricated ink-jet pumps or nozzles similar to those used in ink-jet printers" col.8, lines 24-38 and pumps that deliver 100pL droplets for oligonucleotide synthesis in two dimensional arrays, col. 8, lines 53-67. Similar to the Zebala reference, the laser printer is merely used to pre-structure a solid support that is later used for combinatorial synthesis.

The entire method in Blanchard is directed to the high surface tension solvent and to the formation of droplets for the ink jet pump. See Blanchard col. 3, lines 57-64; col. 3 lines 66-67 to col. 4, lines 1-6; col. 4, lines 7-11, col. 4, lines 30-36 and others. While both Blanchard and the invention use a deprotection method,

different paper or polystyrene base supports, such method and derivatized array supports are not the core of the present invention. The present invention is based on the intermittent immobilization of the monomers within a solid solvent. There is no teaching nor motivation or suggestion in Blanchard to using the phase shift from the solid to liquid in the manner claimed and to carry out the transfer by later printing.

The instant invention claims embedding monomers in a solid solvent thus forming transport units to be addressed to a support. The monomers are immobilized within the solid solvent, Subsequent applications of different monomers in a solid state of aggregation are carried out Once all the different monomers in their transport units have been applied to the support they are then mobilized by melting them or by applying other physical energy to mobilize them The mobilized monomers are then linked to, let's say, free amino groups on the support. Repeating the steps and washing away in between of non-linked particles and other remnants results in the synthesis of a peptide array. The particles are sent using a laser printer. In short, the particles are delivered one after the other to their destination by a laser printer method and then are mobilized by heating them.

According to the foregoing discussion, Blanchard does not render the claims 75, 80 and 87 in the application obvious. Since the claims that depend directly or indirectly from these claims include each and every element of the independent claims, the dependent claims are likewise not rendered obvious by the Blanchard reference.

Withdrawal of the rejection of claims under 35 U.S.C. §102(e), in the alternative under 35 U.S.C. §103(a) over the Blanchard reference is respectfully requested.

REJECTION OF CLAIMS 56-60, 66-67, 69-71, 75, 78-84, 86 AND 87 UNDER 35 U.S.C. §103(a) AS BEING OBVIOUS OVER BLANCHARD IN VIEW OF ZEBALA AND ANDERSON.

At the outset it is noted that the Anderson reference has been overcome as prior art since applicant has perfected its priority and the priority date of applicant antedates the Anderson reference.

The rejection is respectfully traversed.

The Blanchard differences were also discussed in detail under the previous heading. Now the Examiner pulls up Zebala and Anderson to fill in the perceived missing elements of Blanchard. However, a combination of Blanchard and Zebala do not teach the present invention. Both Blanchard and Zebala do not teach the laser printer method in the manner as claimed and the Anderson reference cannot add anything to the combination of Blanchard and Zebala since it is no longer valid as a reference.

With respect to the Examiner's statement that in col. 8, lines 15-18 Blanchard discloses application of a laser printer with a soluble toner, evaporation or by a photolithographic process, applicant responds that a laser printer is merely and explicitly used to pre-structure a solid support for later use in the combinatorial synthesis NOT for addressing monomers to the surface for combinatorial synthesis.

The Examiner admits that Blanchard does not disclose a matrix by which the nucleic acid is embedded including the solvent at a temperature of less than 90°C etc. (see page 18 OA). Therefore the Examiner uses the Zebala reference as supplying those elements. As far as understood, the Examiner claims that the films as disclosed by Zebala are supposed to swell forming a polymeric gel, such that if a particular group of ligands were to bind to the gel, their activity would be visible around that group and the position of the element would reveal the composition of the ligand. How that translates to the elements of applicant claims is not understood. Zebala's invention is obviously in a support with an especially large surface area that has nothing to do with monomers that are embedded in particles.

The Examiner states that Blanchard discloses application of a reagent to the wells using an inkjet printer, laser printer with soluble toner, evaporation or by a photolithographic process. However, similar to Zebala, a laser printer is merely and explicitly used to pre-structure a solid support NOT for addressing the monomers to the surface for combinatorial synthesis.

Like Blanchard, Zebala does not use laser printing. Zebala refers to a lithographic methods. Blanchard refers to an ink jet method. All lithographic methods have severe drawbacks as also outlined in the description. In all lithographic methods a surface of the substrate is patterned into two kinds of areas, namely areas with protecting groups removed to allow for a chemical reaction and areas where the protecting groups are not removed thus hindering chemical reaction. Zebala is not directed to positioning at different times a pattern of different immobilized peptide or nucleic acid monomers in the form of transport units at a solid state of aggregation to a support, which transport units differ from

each other by the monomers immobilized within; wherein the immobilized peptide or nucleic acid monomers are temporarily blocking a coupling reaction of the monomers to the support by the reversibly immobilized monomers; inducing a change in the transport units form the solid state of aggregation to a liquid state of aggregation, thereby permitting a free diffusion of the monomers; then carrying out a coupling reaction to couple at least two different of the monomers to the support at the same time in one single combinatorial synthesis.

Therefore, The combination Blanchard/Zebala does not render claims 75, 80 and 87 nor are the claims dependent from these claims obvious. Should the Examiner disagree with the latter, it is respectfully requested that the rejection under 35 U.S.C. §103(a) is being presented in detail so applicant can respond to the specific elements the Examiner considers obvious.

Withdrawal of the rejection of claims 75, 80 and 87 and the claims depending therefrom under 35 U.S.C. §103(a), is thus respectfully requested.

CONCLUSION

Applicant believes that when reconsidering the claims in the light of the above comments, the Examiner will agree that the invention is in no way properly met or anticipated or even suggested by any of the references however they are considered.

None of the references, nor a combination thereof disclose a method for the combinatorial synthesis as claimed.

In view of the above presented remarks and amendments, it is respectfully submitted that all claims on file should be considered patentably differentiated over the art and should be allowed.

Reconsideration and allowance of the present application are respectfully requested.

Should the Examiner consider necessary or desirable any formal changes anywhere in the specification, claims and/or drawing, then it is respectfully requested that such changes be made by Examiner's Amendment, if the Examiner feels this would facilitate passage of the case to issuance. If the Examiner feels that it might be helpful in advancing this case by calling the undersigned, applicant would greatly appreciate such a telephone interview.

Respectfully submitted,

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